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37. The methods of Claim 35, wherein said MSH or MSH analog compound is selected from the group consisting of α-MSH, β-MSH and γ-MSH.

REMARKS

Claims 1 – 5, 15, 16, 19, 20 and 22 – 29, and 35 – 37 are pending.

Claims1 – 5, 15 and 16 are allowed.

Amended Claims

Applicants have amended claims 19, 22, 37 and 37. No new matter is added in these amendments. Support for the amended claims is found in the specification at the following pages:

claim 19 - page 75, lines 12-23 and page 76, line 23 to page 77, line 18.

claim 22 - page 76 at line 24 to page 77 at line 18.

claim 35 - page 74 at line 20 to page 75 at line 26 and page 32 at lines 24 – 27.

claim 37 - page 21 at lines 12-15.

Rejection of Claims Under 35 U.S.C. §112, first paragraph

The remaining rejections rest on whether, at the time of filing, MC1-R and MC3-R were known as peripheral receptors with the ability to stimulate lipolysis and/or inhibit fatty acid uptake by adipocytes, and in particular, to control obesity. Although the specification provides *in haec verba* support for MC2-R and MC5-R; it also supports a broader disclosure as discussed in detail below.

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1. Written Description Requirement Rejection

Claims 19 – 20, 22 – 29, and 30 -38 stand rejected under 35 U.S.C. §112, first paragraph, for failing to satisfy the written description requirement. In order to put the claims in condition to be allowed or to place them in better condition for appeal, the Applicants have cancelled claims 30 – 34 and 38 without prejudice or disclaimer of the subject matter claimed therein. Applicants have also amended claims 19, 22, 35, and 37 as described above.

The Examiner agrees that the melanocortin receptors MC1-R through MC5-R are described in the specification. However, the Examiner alleges that there is no other disclosure that any melanocortin receptor other than MC2-R and MC5-R was a peripheral receptor with a role in regulating body weight and energy homeostasis.

A. Applicants disclosure teaches all peripheral receptors

At the time of Applicants' invention, pharmacological evidence pointed to the importance of a melanocortinic pathway in the central regulation (i.e. via the central nervous system) of energy balance, as described in the specification on page 6 at lines 18 to 20. Applicants disclosed the importance of a melanocortinic pathway in the peripheral regulation of energy balance. Throughout the specification, Applicants compare such peripheral action with central regulation, via an effect on feed intake, through the MC4-R receptor. For example, on page 25 at line 25 to page 26 line 19, Applicants state that the body weight of an animal can be regulated in the absence of significantly affecting the appetite of

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the animal by a POMC compound administered peripherally in an amount effective to act on peripheral receptors while mitigating effects on central receptors.

Applicants submit that one embodiment of present disclosure describes a method to identify compounds which regulate body weight in an animal. The method described in the specification on page 65 at lines 1 to 10 includes selecting compounds which preferentially bind to and/or activate peripheral melanocortin receptors, particularly as compared to MC4-R.

On pages 76 to 77 of the specification, the Applicants describe assays to identify compounds that selectively agonize or antagonize peripheral melanocortin receptors. The Applicants also describe how such assays may be used to identify compounds that specifically or selectively regulate peripheral melanocortin receptor activity with respect to other melanocortin receptors, and particularly, the central receptor.

B. At the time of filing, skilled artisans recognized MC1-R, MC2-R, MC3-R, and MC5-R as peripheral receptors

Since the Examiner agrees that MC2-R and MC5-R are peripheral receptors, Applicants submit only the following references showing that MC1-R and MC3-R where also known by those skilled in the art to be peripheral receptors[1]:

[1] None f these references teach the role of peripheral receptors in regulating body weight and energy homeostasis. This is described for the first time in applicant's disclosure.

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B.1 MC1-R

U.S. Patent 5,908,609, column 2 at lines 15 to 17, states that MC1-R is expressed in melanocytes,

B2 MC3-R

U.S. Patent 5,710,265, column 5 at lines 28 to 30, states that MC3-R is expressed in gut tissues;

Chagnon, Y.C. et al. Mol. Med 3, 663-673 (1997) state that MC3-R is expressed in adipose tissue and the heart;

Chhajlani, V. Biochem. Mol. Biol. Int. 38, 73 – 80 (1996) states that MC3-R is expressed in the heart, mammary gland, ovary, skeletal muscle and the kidney;

Gantz, I. et al. J. Biol. Chem. 268 8246 – 8250 (1993) state that MC3-R is expressed in the stomach, duodenum, placenta and pancreas.

Applicants submit that those skilled in the art, upon reading the Applicants' specification, would immediately recognize that Applicants' test methods disclose a method of identifying compounds that selectively or selectively regulate the MC1-R, MC2-R, MC3-R, or MC5-R receptors. Applicants also disclose test methods for identifying those compounds that do so without significantly affecting the appetite by stimulating the MC4-R receptor.

C. No *in haec verba* support in the specification is required

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In order to comply with the written description requirement, the specification need not describe the claimed subject matter in exactly the same terms as used in the claims; it must simply indicate to persons skilled in the art that as of the filing date the applicant had invented what is claimed. Eiselstein v. Frank, 52 F.3d 1035, 1038, 34 USPQ2d 1467, 1470 (Fed. Cir. 1995). Applicants submit that their disclosure describes the class of melanocortin receptors MC1-R to MC5-R and also that MC4-R is accepted as the "central nervous system" receptor. Applicants also describe assays allowing the identification of compounds that agonize or antagonize the peripheral receptors to a significantly greater degree than they agonize or antagonize the MC4-R receptor.

Therefore, Applicants are entitled to claim a method of using each of MC1-R, MC2-R, MC3-R, and MC5-R. Applicants have chosen to claim MC2-R and MC5-R in claims 1-6 and 15-16. Claims 19-20, and 22- 25 are directed to MC1-R and MC3-R.

For the reasons stated above, Applicants request that the Examiner withdraw his 35 U.S.C. §112, first paragraph, written description requirement rejection.

2. Enablement Requirement Rejection

Claims 19 – 20, 22 – 29, and 30 -38 stand rejected under 35 U.S.C. §112, first paragraph, for failing to satisfy the scope of the enablement requirement. The Examiner alleges that although the specification discloses melanocortin receptors MC1-R through MC5-R, the Applicants recognized only MC2-R and/ or

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MC5-R to be the peripheral receptors with the ability to stimulate lipolysis and/or inhibit fatty acid uptake by adipocytes, and in particular, to control obesity. The Examiner states that, given the breadth of claims 19 – 20 and 22 – 29 in light of the unpredictability of the art, the amount of experimentation required to make and/ or use the full scope of the claimed receptors would require undue trial and error experimentation.

As discussed with respect to the Examiner's written description rejection, Applicants submit that their specification discloses assays allowing the identification of compounds that selectively or selectively regulate the receptors MC1-R, MC2-R, MC3-R, or MC5-R, particularly those compounds that do so without significantly affecting the appetite by stimulating the MC4-R receptor. Pages 65 to 78 of Applicants disclosure contains a detailed description of a number of such assay methods.

In the above discussion, Applicants have discussed the state of the art at the time of the invention. MC4-R was widely recognized by those skilled in the art as, and is described in Applicants' specification as, the "central nervous system" receptor. The other melanocortin receptors were widely recognized as peripheral melanocortin receptors and are also described in the Applicants' specification.

Applicants also describe the peripheral regulation of body weight and energy homeostasis. In addition, they specifically describe assay methods allowing the identification of compounds selectively or selectively regulate the other four melanocortin receptors to a significantly greater degree than they

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regulate the MC4-R receptor. In view of this disclosure, Applicants submit that they have met the enablement requirement with respect to the claims in dispute.

For the reasons stated above, Applicants request that the Examiner withdraw his 35 U.S.C. §112, first paragraph, enablement requirement rejection.

Attached hereto is a marked up version of the changes made to the claims. In reply to the Office Action dated September 25th, 2002, favorable reconsideration and allowance of this application are respectively requested for the reasons set forth in the above remarks. If, for any reason, the Examiner is unable to allow the application and feels that an interview would be helpful to resolve any remaining issues, he is respectfully requested to contact the undersigned attorney at (312) 321-4229.

Respectfully submitted,

Dated: November 25th, 2002.

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VERSION WITH MARKINGS TO SHOW CHANGES MADE.

IN THE CLAIMS

19. (Three times amended) A method for identifying compounds that regulate peripheral pathways of energy homeostasis, comprising:

a. contacting a putative regulatory compound with an isolated adipocyte; and,

b. detecting putative regulatory compounds that bind to a melanocortin receptor on said adipocyte, wherein said melanocortin receptor is selected from a group consisting of a MC1-R[,] and a MC3-R[, or MC5-R] receptor, and wherein putative regulatory compounds that bind to said melanocortin receptor on said adipocytes are identified as compounds that regulate body weight by regulating peripheral pathways of energy homeostasis.

22. (Twice amended) A method for identifying compounds that preferentially bind to and activate peripheral melanocortin receptors comprising:

a. contacting a putative regulatory compound with a cell which expresses a peripheral melanocortin receptor selected from a group consisting of MC1-R[, MC2-R,] and MC3-R [and MC5-R];

b. detecting whether the putative regulatory compound increases activity of said melanocortin receptor;

c. contacting said putative regulatory compound with a cell which expresses a melanocortin 4-receptor (MC4-R); and

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d. detecting whether the putative regulatory compound increases MC4-R activity;

wherein putative regulatory compounds that induce greater activity by said peripheral melanocortin receptor as compared to said MC4-R are identified as compounds that preferentially bind to and activate peripheral melanocortin receptors.

35. (Amended) A method for identifying compounds that increase body weight by regulating peripheral pathways of energy homeostasis, comprising:

a. contacting a cell which expresses a peripheral melanocortin receptor [selected from the group consisting of MC1-R, MC3-R and MC5-R] with [proopiomelanocortin (POMC)] a MSH or a MSH analog compound which binds to and activates said melanocortin receptor in the presence and absence of a putative regulatory compound;

b. detecting whether said putative regulatory compound inhibits said melanocortin receptor activity;

wherein putative regulatory compounds that inhibit said melanocortin receptor activity are identified as compounds that increase body weight by regulating peripheral pathways of energy homeostasis.

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37. (Amended) The methods of Claim 35, wherein said [POMC] MSH or MSH analog compound is [a melanocortin compound] selected from the group consisting of α-MSH, β-MSH and γ-MSH.